

US009409981B2

(12) United States Patent

LaVallie et al.

(54) ANTIBODY TO GDF8 AND USES THEREOF

(71) Applicant: **Pfizer Inc.**, New York, NY (US)

(72) Inventors: Edward Roland LaVallie, Harvard, MA (US); Lisa Anne Collins-Racie, Acton,

MA (US); Christopher John Corcoran, Arlington, MA (US); Lioudmila Gennadievna Tchistiakova, Andover, MA (US); John Adam Nowak, Stratham, NH (US); Riyez Karim, North Andover, MA (US); Xiang-Yang Tan, Reading, MA (US); Kimberly Ann Marquette, Somerville, MA (US);

Geertruida Machteld Veldman,

Sudbury, MA (US)

(73) Assignee: **Pfizer Inc.**, New York, NY (US)

(*) Notice: Subject to any disclaimer, the term of this

patent is extended or adjusted under 35

U.S.C. 154(b) by 0 days.

(21) Appl. No.: 13/791,700

(22) Filed: Mar. 8, 2013

(65) **Prior Publication Data**

US 2014/0023638 A1 Jan. 23, 2014

Related U.S. Application Data

- (62) Division of application No. 12/262,712, filed on Oct. 31, 2008, now Pat. No. 8,415,459.
- (60) Provisional application No. 61/001,783, filed on Nov. 1, 2007.
- (51) Int. Cl.

 A61K 39/00
 (2006.01)

 A61K 39/395
 (2006.01)

 C07K 16/22
 (2006.01)

(52) U.S. Cl.

(58) Field of Classification Search

None

See application file for complete search history.

(56) References Cited

PUBLICATIONS

McPherron et al., 1997, Nature 387:83-90.*

Whittemore et al., 2003, Biochem. Biophys. Res. Commun. 300:965-071 *

Bogdanovich et al., 2002, Nature 420:418-421.*

Kim et al., 2001, Biochem. Biophy. Res. Commun. 281:902-906.*

McPherron et al., 2002, J. Clin. Invest. 109:565-601.*

Hamrick et al., 2000, Bone 27:343-349.*

International Preliminary Report on Patentability from PCT/US2008/012338 (WO2009/058346 Mailed May 4, 2010.

Haffar et al. Topogenic Analysis of the Human Immunodeficiency Virus Type 1 Envelope Glycoprotein, p. 160 in Microsomal Membranes, J. Cell Biol., 107:1677-1687, 1988. (10) Patent No.: US 9,409,981 B2

(45) **Date of Patent:**

Aug. 9, 2016

Wagner et al., A Phase I/II Trial of MYO-029 in Adult Subjects with Muscular Dystrophy, Ann. Neurol., 63: 561-71, 2008.

Kingsley, David M. et al., "The TGF-β superfamily: new members, new receptors, and new genetic tests of function in different organisms," 1994, Genes & Development, vol. 8, pp. 133-146.

Hoodless, P.A. and Wrana, J. L., "Mechanism and Function of Signaling by the TGFβ Superfamily," 1998, Current Topics in Microbiology and Immunology, vol. 228, pp. 235-272.

Miyazono, Kohei et al., "Latent High Molecular Weight Complex of Transforming Growth Factor β1 Purification From Human Platelets and Structural Characterization," 1988, Journal of Biological Chemistry, vol. 263, pp. 6407-6415.

Wakefield, Lalage M. et al., "Latent Transforming Growth Factor-62 from Human Platelets A High Molecular Weight Complex Containing Precursor Sequence," 1988, Journal of Biological Chemistry, vol. 263, pp. 7646-7654.

Brown, Peter D. et al., "Physicochemical Activation of Recombinant Latent Transforming Frowth Factor-beta's 1, 2, and 3," 1990, Growth Factors, vol. 3, pp. 35-43.

Thies, R. Scott et al., "GDF-8 Propeptide Binds to GDF-8 and Antagonizes Biological Activity by Inhibiting GDF-8 Receptor Binding," 2001, Growth Factors, vol. 18, pp. 251-259.

Gentry, Larry E. et al., "The Pro Domain of Pre-Pro-Transforming Growth Factor 131 When Independently Expressed Is a Functional Binding Protein for the Mature Growth Factor," 1990, Biochemistry, vol. 29, pp. 6851-6857.

Derynck, Rik et al., "Human transforming growth factor-13 complementary DNA sequence and expression in normal and transformed cells," 1995, Nature, vol. 316, pp. 701-705.

Massague, Joan, "The Transforming Growth Factor-62 Family," 1990, Annual Review of Cell Biology, vol. 6, pp. 597-641.

Gamer, Laura W. et al., "A Novel BMP Expressed in Developing Mouse Limb, Spinal Cord, and Tail Bud Is a Potent Mesoderm Inducer in Xenopus Embryos," 1999, Developmental Biology, vol. 208, pp. 222-232.

McPherron, Alexandra C. and Lee, Se-Jin, "Double muscling in cattle due to mutations in the myostatin gene," 1997, Proceedings of the National Academy of Science U.S.A. vol. 94, pp. 12457-12461. Lee, Se-Jin and McPherron, Alexandra C., "Myostatin and the control of skeletal muscle mass," 1999, Current Opinion in Genetics & Development, vol. 9, pp. 604-607.

(Continued)

Primary Examiner — Elizabeth C Kemmerer

(57) ABSTRACT

The disclosure provides novel molecules related to growth and differentiation factor 8 (GDF8), in particular epitopes specific to GDF8 and other specific antagonists of GDF8 in particular anti GDF8 antibodies or antigen binding protein or fragment thereof which may inhibit GDF8 activity and signal in vitro and/or in vivo. The disclosure also provides for an immunoassay used to detect and quantitate GDF8. The disclosure also provides methods for diagnosing, preventing, ameliorating, and treating GDF8 associated disorders, e.g., degenerative orders of muscle, bone, and insulin metabolism. Finally, the disclosure provides pharmaceuticals for the treatment of such disorders by using the antibodies, polypeptides, polynucleotides, and vectors of the invention.